

- I. Relative Rates of Oxidation of Ortho,
Meta and Para Compounds.
- II. Orthosulphaminebenzoic Acid and
Related Compounds.
- III. Some Derivatives of Phenylglyco-
collorthosulphonic Acid.

DISSERTATION

SUBMITTED TO THE BOARD OF UNIVERSITY STUDIES OF
THE JOHNS HOPKINS UNIVERSITY IN CONFORMITY
WITH THE REQUIREMENTS FOR THE DEGREE
OF DOCTOR OF PHILOSOPHY.

BY

HAMILTON BRADSHAW.

1905

EASTON, PA. :
ESCHENBACH PRINTING COMPANY.

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PART I.

RELATIVE RATES OF OXIDATION OF ORTHO, META AND PARA COMPOUNDS.

In 1887 Dreyfus¹ determined the rate at which various organic compounds are oxidized by potassium permanganate. If n grams of a substance are required to reduce a quantity of potassium permanganate equal to that reduced in the same length of time by 1 gram of ethyl alcohol, then $1/n$ expresses, in a manner, the relative rate of oxidation of the substance. Dreyfus made his measurements in acid solution and used a very dilute solution of potassium permanganate, 1 cc = 0.0001 gram of crystallized oxalic acid. He found that the value of $1/n$ for the substances which he studied varies from 0.2 to 10,000. With the dihydroxybenzenes the rates of oxidation are in the ratio—ortho : meta : para : : 5000 : 2000 : 3333. For the toluidines he found the ratio—ortho : meta : para : : 17.8 : 9.09 : 12.5.

The present investigation was undertaken to determine the rates of oxidation of certain isomeric organic compounds of the ortho, meta and para series. It was thought that a comparison of the behavior of several groups of such isomeric compounds might possibly reveal some tendency which would admit of general expression.

The compounds which were studied for this purpose are all easily prepared. Those that were obtained from the laboratory stock were purified by crystallization or distillation. The following is a list of the substances used, together with their melting-points (uncorr.) :

	Melting point.
Salicylic acid	155°–156°
<i>m</i> -Hydroxybenzoic acid	198°–199°
<i>p</i> -Hydroxybenzoic acid	210°
Anthranilic acid	145°
<i>m</i> -Aminobenzoic acid	173°
<i>p</i> -Aminobenzoic acid	186°

¹ Compt. rend., 105, 523.

	Melting point.
<i>o</i> -Nitrophenol	45°-46°
<i>m</i> -Nitrophenol	95°-96°
<i>p</i> -Nitrophenol	112°-113°
<i>o</i> -Nitriline	73°-74°
<i>m</i> -Nitriline	112°
<i>p</i> -Nitriline	147°
<i>o</i> -Toluidine	
<i>m</i> -Toluidine	
<i>p</i> -Toluidine	45°

Parahydroxybenzoic acid was made by fusing parasulphaminebenzoic acid with a mixture of sodium and potassium hydroxides.

Of all these substances, except the nitrilines, aqueous solutions were made, containing 1 gram to the liter. Only 0.5 gram of the nitrilines was dissolved in a liter of water, on account of the slight solubility of these compounds, but twice as much of the solution was used in each experiment. The toluidines were dissolved by adding sufficient sulphuric acid to form the neutral salts. The solution of potassium permanganate used for the oxidations contained 4 grams of potassium permanganate to a liter of water. The procedure was as follows: A fixed amount of the solution of the organic substance was diluted to a definite volume and a quantity, usually 15 cc., of the solution of potassium permanganate was added from a burette. After allowing the mixture to stand for a certain length of time, the excess of potassium permanganate was determined. At first this was done by adding an excess of a solution of manganous sulphate, free from iron, and filtering off the precipitated oxides of manganese on an asbestos plug. By dissolving in a known quantity of a standard solution of oxalic acid, or of ferrous ammonium sulphate, and titrating the excess of reducing substance, the amount of available oxygen in the precipitate was determined and, by subtraction, the oxygen used in the oxidation of the organic compound.

It was found, however, that this method does not give satisfactory results, probably on account of a loss of oxygen in

heating the solution to dissolve the oxides of manganese. The method finally decided upon for the determination of the un-reduced potassium permanganate, is that based on the liberation of iodine from potassium iodide by potassium permanganate, in the presence of an acid. At the end of the oxidation period, an excess of a solution of potassium iodide and dilute hydrochloric acid was added to the mixture, and the liberated iodine determined by titration with a solution of sodium thiosulphate, previously standardized against the solution of potassium permanganate by the same method.

In the case of the nitranilines the end product was not very definite. Apparently some oxidation product continued to liberate iodine and, consequently, the quantity of thiosulphate used was too great, although the titrations were made as rapidly as possible. The figures expressing the amounts of potassium permanganate reduced are, therefore, uniformly low for this group of compounds.

The oxidations were made at room temperature, which varied from 18° to 22° .

Hydroxybenzoic Acids.

The first group studied was that of the hydroxybenzoic acids. Measurements were made on solutions to which neither acid nor alkali had been added. The results are given in tabular form. In this and the following tables the quantity of potassium permanganate, reduced by the organic substance, is expressed as cubic centimeters of solution. For the sake of convenience, the reduction is regarded as being complete, that is, to the manganous condition.

Table I.—Oxidation of Hydroxybenzoic Acids.

0.005 gram $C_7H_6O_3$, 15 cc. $KMnO_4$, total volume 100 cc.

$KMnO_4$ reduced, cc.

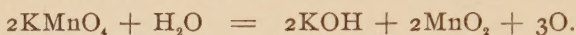
Time in minutes.	Ortho.	Meta.	Para.
1	. .	0.46	0.24
2	1.37	0.94	0.37
5	1.85	1.50	0.69
10	2.23	1.99	1.27
20	2.75	2.57	1.91
30	3.18	2.83	2.37
60	3.51	3.47	3.37
120	3.86	4.53	4.64
1080	5.50	6.00	6.22

Numerous other experiments were made, varying the quantity of substance, of potassium permanganate and of water. The general result was always the same, that is, the ortho compound was most readily oxidized, the para compound least readily. The differences were, in a few cases, greater than those tabulated above, but were of the same general character. The effect of a greater excess of permanganate is very slight, unless its concentration be increased.

Complete oxidation of the hydroxybenzoic acids according to the equation,



would require for 0.005 of acid, 0.053 gram of potassium permanganate, yielding its oxygen according to the equation



The quantity of solution used, 15 cc., contained 60 milligrams of potassium permanganate.

A study was also made of the effect of the addition of varying amounts of acid or alkali to the solution. The results are brought together in Table II. The first column contains the number of equivalents of acid or alkali added to the solution. For example, the addition of 2 equivalents of acid or alkali means the addition of 1 molecule of sulphuric acid or 2 molecules of potassium hydroxide for every molecule of hydroxybenzoic acid in the solution.

Table II.—Oxidation of Hydroxybenzoic Acids.

0.005 gram $\text{C}_7\text{H}_6\text{O}_3$, 15 cc. KMnO_4 , total volume 100 cc.

	KMnO ₄ reduced, cc.					
	Ortho.		Meta.		Para.	
	2 min.	5 min.	2 min.	5 min.	2 min.	5 min.
20 acid	.	5.40	.	5.80	.	4.99
4 "	4.57	5.04	.	5.27	.	2.89
2 "	3.47	3.90	.	4.00	.	1.93
0 "	1.37	1.85	0.94	1.50	0.37	0.69
1 alkali	0.51	0.65	0.25	0.40	0.20	0.37
2 "	0.17	0.50	3.65	4.07	1.79	2.99
4 "	0.63	1.35	3.90	4.28	1.62	2.87
10 "	1.70	.	3.53	.	1.22	.
20 "	2.36	3.05	3.30	3.96	1.15	1.59

In order to determine whether the effect of the addition of potassium hydroxide depends on the actual quantity of alkali in the solution, or on its concentration, measurements were made on solutions diluted with varying quantities of water. In the following table the figures at the head of the columns refer to the total volume of the solution.

Table III.—Oxidation of Hydroxybenzoic Acids.

0.005 gram $C_7H_6O_3$, 15 cc. $KMnO_4$, time 2 minutes.

	$KMnO_4$ reduced, cc.				
	Ortho.		Meta.		
	50 cc.	100 cc.	50 cc.	100 cc.	150 cc.
1 acid	. .	. .	3.07	. .	. .
0 "	2.34	1.37	1.96	0.94	0.37
1 alkali	1.44	0.51	4.16	0.25	0.14
2 "	1.63	0.17	4.34	3.65	0.24
4 "	1.89	0.63	4.43	3.90	3.20
6 "	2.23	. .	4.42	. .	. .
10 "	. .	1.70	. .	3.53	. .
12 "	2.84	. .	. .	. .	. .
20 "	. .	2.36	. .	3.30	2.61

A careful study of these results leads to the conclusion that the effect of the alkali depends on its concentration in the solution, and not on the actual quantity present. For example, in the first column the point of minimum oxidation corresponds to the presence of a carboxyl salt, while in the second column the same point is reached only when sufficient alkali is present to form a neutral salt.

By separate experiments it was shown that sodium hydroxide has exactly the same effect as potassium hydroxide, and that the presence of corresponding quantities of potassium or sodium chloride has no influence whatever on the rate of oxidation.

During the process of oxidation the solution becomes alkaline, unless the potassium hydroxide, formed by the reduction of the potassium permanganate, is neutralized by acid oxidation products of the organic substance. It was found that considerable quantities of oxalic acid are formed when salicylic

acid is oxidized by potassium permanganate. Acetic acid is known to be a frequent oxidation product of aromatic compounds. In view of the uncertainty arising from these facts, and also from a consideration of the results presented in Table II., it seemed more satisfactory to start with solutions made alkaline by the addition of considerable quantities of potassium hydroxide. Table IV. contains the results obtained by oxidation in alkaline solution.

Table IV.—Oxidation of Hydroxybenzoic Acids.

0.005 gram $C_7H_6O_3$, 15 cc. $KMnO_4$, 10 equivalents KOH, total volume 100 cc.

Time in minutes.	KMnO ₄ reduced, cc.		
	Ortho.	Meta.	Para.
2	1.70	3.53	1.22
10	3.25	4.70	2.39
30	4.66	5.25	3.93
60	5.34	5.50	5.02

Aminobenzoic Acids.

Table V.—Oxidation of Aminobenzoic Acids.

0.005 gram $C_7H_7O_2N$, 15 cc. $KMnO_4$, total volume 100 cc.

Time in minutes.	KMnO ₄ reduced, cc.		
	Ortho.	Meta.	Para.
0.5 (at 0°)	1.35	1.24	0.73
1	2.18	2.26	1.59
2	2.41	2.73	1.92
15	2.81	3.67	3.47
340	3.58	4.89	4.89

The first three measurements were made at 0°, because the experiments with the hydroxybenzoic acids show that the ortho compound is most readily oxidized in the first stages of the oxidation. These results with the aminobenzoic acids are exactly analogous to those obtained with the hydroxybenzoic acids. Further measurements were made in alkaline solution.

Table VI.—Oxidation of Aminobenzoic Acids.

0.005 gram $C_7H_7O_2N$, 15 cc. $KMnO_4$, 10 equivalents KOH ,
total volume 100 cc.

Time in minutes.	$KMnO_4$ reduced, cc.		
	Ortho.	Meta.	Para.
2	1.90	2.78	1.12
10	3.33	4.67	2.29
30	4.91	6.17	4.28
60	5.94	6.75	4.88

Here also, as with the hydroxybenzoic acids, the order of velocities is meta, ortho, para.

Berkeley¹ found that the rate of reduction of the nitrobenzoic acids by stannous chloride increases from the meta to the para compound. His results seem to harmonize very satisfactorily with the conclusions reached in the present investigation.

Nitrophenols.

The nitrophenols being easily obtained, experiments were tried with them.

Table VII.—Oxidation of Nitrophenols.

0.005 gram $C_6H_5O_3N$, 15 cc. $KMnO_4$, total volume 25 cc.

Time in minutes.	$KMnO_4$ reduced, cc.		
	Ortho.	Meta.	Para.
1	1.05	0.78	0.36
5	2.25	1.75	0.68
30	5.60	5.15	3.01

Table VIII.—Oxidation of Nitrophenols.

0.005 gram $C_6H_5O_3N$, 20 cc. $KMnO_4$, total volume 30 cc.

Time in minutes.	$KMnO_4$ reduced, cc.		
	Ortho.	Meta.	Para.
90	6.24	6.20	5.90
390	6.80	6.51	6.72

¹ Dissertation, Johns Hopkins University, 1899.

Table IX.—Oxidation of Nitrophenols.

0.05 gram $C_6H_5O_3N$, 15 cc. $KMnO_4$, 10 equivalents KOH, total volume 50 cc.

Time in minutes.	$KMnO_4$ reduced, cc.		
	Ortho.	Meta.	Para.
10	0.42	1.84	0.30
30	1.12	3.27	0.35
60	1.51	4.33	0.69
120	2.15	4.67	0.91

The results with solutions of the free nitrophenols are similar to those obtained for the two preceding groups. Here also, in alkaline solution, the order of velocities is meta, ortho, para.

*Nitranilines.**Table X.—Oxidation of Nitranilines.*

0.005 gram $C_6H_5O_2N_2$, 15 cc. $KMnO_4$, total volume 25 cc.

Time in minutes.	$KMnO_4$ reduced, cc.		
	Ortho.	Meta.	Para.
10	0.22	2.94	0.22
60	0.91	4.04	0.43
10 (at 100°)	5.08	5.82	3.15

Table XI.—Oxidation of Nitranilines.

0.005 gram $C_6H_5O_2N_2$, 15 cc. $KMnO_4$, 10 equivalents KOH, total volume 35 cc.

Time in minutes.	$KMnO_4$ reduced, cc.		
	Ortho.	Meta.	Para.
30	1.12	4.23	0.84
60	1.35	4.52	0.89
120	2.53	4.91	1.22
360	3.02	5.19	1.71

Both of these tables show the same order in the rates of oxidation of the nitranilines, namely, meta, ortho, para.

*Toluidines.**Table XII.—Oxidation of the Toluidines.*

0.005 gram C_7H_9N , 15 cc. $KMnO_4$, 10 equivalents KOH ,
total volume 100 cc.

Time in minutes.	$KMnO_4$ reduced, cc.		
	Ortho.	Meta.	Para.
0.5	3.94	4.28	2.55
1	4.28	4.75	2.72
2	4.69	5.13	3.03
5	5.30	5.61	3.51

In acid solution the oxidation was rapid and nearly equal for all 3 isomers.

In all 5 groups a uniformity is shown only in alkaline solution. The differences in the rates of oxidation of isomeric substances are quite marked and the rate of oxidation decreases from the meta to the para compound.

PART II.

ORTHOSULPHAMINEBENZOIC ACID AND RELATED COMPOUNDS.

A few years ago F. D. Wilson, working in the laboratory of the Johns Hopkins University, made a comparative study of

orthosulphaminebenzoic acid, $C_6H_4 \begin{matrix} \diagup COOH \\ \diagdown SO_2NH_2 \end{matrix}$, and orthocarba-

minebenzenesulphonic acid, $C_6H_4 \begin{matrix} \diagup CONH_2^1 \\ \diagdown SO_2OH \end{matrix}$. As a few points

were left unsettled I have continued the work.

Wilson states that orthosulphaminebenzoic acid crystallizes in two forms, plates and needles, and that the quantity of alkali used in the hydrolysis of the benzoic sulphinide determines which form the acid will take on crystallization.

¹ Am. Chem. J., 30, 353 and Dissertation.

Several experiments were made to test this point. Wilson boiled a solution of 20 grams of benzoic sulphinide with 15 grams of sodium hydroxide, in 500 cc. of water, until hydrolysis was complete. The solution was acidified and allowed to stand over night. Large, monoclinic crystals were deposited. In repeating this work it was found that complete hydrolysis was not reached even after 15 hours' boiling. After cooling and filtering, the solution was acidified with hydrochloric acid. Only needles were deposited. Another alkaline solution, obtained in exactly the same way, was divided into two portions. One part of it was acidified and allowed to stand. Both forms of crystals began to appear, but on agitating the solution the plates ceased to form and the acid came down in needles. The second portion was acidified and seeded with plate crystals. All of the acid was deposited in the form of plates. In another experiment Wilson used 10 grams of benzoic sulphinide to 20 grams of sodium hydroxide and 250 cc. of water. This solution, treated in the same way as the previous one, gave only needles, the yield being almost quantitative. In the first experiment in which these proportions were used, Wilson's conclusions were confirmed, that is, only needles were obtained. In the second, a few plate crystals formed among the needles. Moreover, it was found that this proportion of alkali caused complete hydrolysis in less than 3 hours.

To determine whether the presence of benzoic sulphinide would induce the formation of plate crystals, the next solution of the hydrolyzed benzoic sulphinide was divided into two portions. To one, benzoic sulphinide was added until the solution tasted sweet. When acidified, the solution deposited most of the acid in needles, only a few plates being formed. The second portion of solution, containing no benzoic sulphinide, yielded only large plate crystals. From these experiments it is evident that the form of the crystals does not depend on the quantity of alkali used, nor on the presence of benzoic sulphinide. It is very probable that the plate crystals are formed only when the acidified solution suffers the least possible disturbance. Similar relations are known to hold with many other substances.

As stated by Wilson, the plate form of the acid contains no water of crystallization, while the needle crystals lose 0.5 molecule of water of crystallization at 100° – 110° .

	Calculated for $C_6H_4(COOH)SO_2NH_2 \cdot \frac{1}{2}H_2O$.	I.	Found.	II.
H_2O	4.29	4.33		4.25

When crystallized from alcohol the acid is deposited in large rhombohedrons. Another form of crystals was obtained by hydrolyzing 20 grams of benzoic sulphinide with 30 grams of potassium hydroxide, in 500 cc. of water. When acidified, the solution deposited the acid in small, irregular crystals, about 1–2 mm. in diameter. The study of the crystalline form was not considered to be of sufficient importance to justify further investigation. The melting point of the acid, in whatever form it may be crystallized, is 152° (uncorr.).

Orthosulphaminebenzoic acid loses water when heated and is converted, at least partially, into benzoic sulphinide. A portion is probably converted into acid ammonium orthosulphobenzoate, as is the case with parabromorthosulphaminebenzoic acid.¹ Wilson states that in a rapid current of air the needles decompose at 115° , the plates at about 128° , and that, in a closed tube, the needles decompose at 145° , the plates at 135° .

In repeating this work, an apparatus was used similar to that described by Wilson, but the thermometer was placed in the glass tube with the boat, and windows of mica were fixed in the outer casing, to permit the reading of the thermometer and accurate observation of the decomposition. The crystals were powdered before being placed in the boat. It was found that both needles and plates became sweet when heated at 114° – 116° , for 2 hours, either in a rapid current of air or in a closed tube. Very little water collected in the cool part of the tube. Generally a slight sublimate of benzoic sulphinide was noticed.

Wilson's Diamide.

Wilson prepared what he supposed to be the diamide,

¹ Blanchard : *Am. Chem. J.*, **30**, 509.

$\text{C}_6\text{H}_4 \begin{cases} \text{CONH}_2 \\ \text{SO}_2\text{NH}_2 \end{cases}$, by heating orthosulphaminebenzoic acid

with ammonium thiocyanate. By following his directions carefully, a product was obtained which melted at $256^\circ\text{--}257^\circ$ (uncorr.). Wilson gives 263° . It is very soluble in water, insoluble in cold alcohol, more soluble in hot alcohol. It gives off ammonia when treated in the cold with a solution of sodium hydroxide. These facts indicated that the substance is ammonium orthocarbaminebenzenesulphonate.¹ A determination of nitrogen completed the evidence :

0.2450 gram salt gave 0.0315 gram N.

	Calculated for $\text{C}_6\text{H}_4(\text{CONH}_2)\text{SO}_2\text{ONH}_4$.	Found.
N	12.86	12.85

Orthocarbaminebenzenesulphonic Acid.

Potassium orthocarbaminebenzenesulphonate was prepared as directed by Wilson. When this salt is heated with phosphorus oxychloride, a compound is obtained which Wilson supposed to be orthocarbaminebenzenesulphone chloride. He crystallized it from chloroform, and found the melting point to be 63° . By the action of phosphorus pentachloride on the same salt, Sohon² obtained orthocyanbenzenesulphone chloride, which he identified by converting it into orthocyanbenzenesulphonic acid. It seemed very probable that the reaction with phosphorus oxychloride would give the same product. The chloride was prepared as directed by Wilson, and crystallized from chloroform. It melts at $69^\circ\text{--}70^\circ$ (uncorr.). The same substance was then prepared by the action of phosphorus oxychloride on potassium orthocyanbenzenesulphonate. This salt was obtained from the ammonium salt which is formed by the action of ammonia on the unsymmetrical chloride of orthosulphobenzoic acid.³ The chloride obtained in this way melted at $69^\circ\text{--}70^\circ$. Jesurun⁴ prepared the same chloride by heating

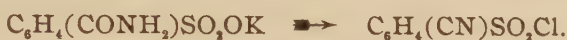
¹ Wilson : *Loc. cit.*, p. 370.

² Am. Chem. J., **20**, 271.

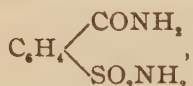
³ *Ibid.*, **30**, 268.

⁴ Ber. d. chem. Ges., **26**, 2288.

benzoic sulphinide with 2 molecules of phosphorus pentachloride, in a sealed tube, at 70° – 75° . He gives the melting point as 69° – 70° . Specimens of the chloride prepared by all three of these methods were found to have the same melting point, 69° – 70° , which was not lowered by mixing one specimen with another. There is no doubt, therefore, that the action of phosphorus oxychloride includes dehydration of the carbamide group,



This explains Wilson's failure to obtain the diamide,



by the action of ammonia on the chloride which he supposed to be orthocarbaminebenzenesulphone chloride. Jesurun¹ describes the action of ammonia on orthocyanbenzenesulphone chloride as follows: If an excess of ammonia is used the

product is pseudosaccharin amide, $\text{C}_6\text{H}_4 \begin{cases} \text{C}(\text{NH})_2 \\ \text{SO}_2 \end{cases} \text{N}$, melt-

ing above 300° . If the chloride is treated with benzene, in which the theoretical quantity of ammonia has been dissolved,

the product is orthocyanbenzenesulphonamide, $\text{C}_6\text{H}_4 \begin{cases} \text{CN} \\ \text{SO}_2\text{NH}_2 \end{cases}$,

melting above 260° . This work was repeated, using the chloride obtained by Wilson's method, and Jesurun's results were confirmed, except in regard to the melting points. Pseudosaccharin amide, when crystallized from hot water, melts at 297° (uncorr.). Analyses:

I. 0.2025 gram substance gave 0.0310 gram N.

II. 0.1722 gram substance gave 0.0267 gram N.

III. 0.2118 gram substance gave 0.2712 gram BaSO_4 .

Calculated for		Found.	
$\text{C}_6\text{H}_4 \begin{cases} \text{C}(\text{NH}_2)_2 \\ \text{SO}_2 \end{cases} \text{N}$		I.	II.
N	15.38	15.30	15.49
S	17.59	..	17.60

¹ Ber. d. chem. Ges., 26, 2296.

Orthocyanbenzenesulphonamide melts at 160° (uncorr.), changing completely, at its melting point, to the isomeric substance, pseudosaccharin amide, which melts at 297° (uncorr.). If heated rapidly no melting is observed at 160° . This explains Jesurun's observation that the substance melts above 260° .

When orthocyanbenzenesulphonamide is heated with a dilute solution of sodium hydroxide, it is converted into benzoic sulphinide. It may be that the diamide is first formed and loses ammonia immediately. The diamide has not yet been prepared.

Anilineorthosulphonic Acid.

This acid can be prepared by the action of sodium hypobromite on an alkaline solution of potassium orthocarbaminebenzenesulphonate. Forty grams of this salt and 32 grams of sodium hydroxide were dissolved in 320 cc. of water. The solution was warmed to 80° on the water-bath, and 28 grams of bromine, dissolved in 220 cc. of a 10 per cent solution of sodium hydroxide, were added drop by drop. The mixture was heated about 15 minutes and, after cooling, was acidified with hydrochloric acid. By evaporating to a very small bulk and filtering while hot, the sodium chloride was removed. The anilineorthosulphonic acid crystallized out on cooling and was obtained pure by recrystallization from hot water. Analysis :

0.0927 gram substance gave 0.1255 gram BaSO_4 .

	Calculated for $\text{C}_6\text{H}_4(\text{NH}_2)\text{SO}_2\text{OH}$.	Found.
S	18.51	18.58

If the sodium hypobromite is added rapidly to a cold solution of the carbamide, the chief product is tribromaniline. This is easily explained by the fact that anilineorthosulphonic acid is readily converted into tribromaniline by the action of free bromine.¹ If the sodium hypobromite is added slowly to a cold solution of the carbamide, the product is parabromanilineorthosulphonic acid. Even under the most favorable con-

¹ Berendsen and Limpricht : Ann. Chem. (Liebig), 177, 100 (1875).

ditions some of this acid is formed. It is very insoluble in cold water and can be removed by filtration.

PART III.

SOME DERIVATIVES OF PHENYLGLYCOCOLL- ORTHOSULPHONIC ACID.

Anilineorthosulphonic Acid.

The preparation of this acid from orthocarbaminebenzenesulphonic acid has been described in the preceding section. This method, including the preparation of the carbamine acid, was too laborious for the production of the acid in any considerable quantity, and the method of Kreis¹ was tried, with good results. Acetanilide was brominated in glacial acetic acid solution², and the product was crystallized from alcohol. The directions of Kreis were followed in the sulphonation of the parabromacetanilide. There was considerable charring and the yield was never better than 65 per cent of the theoretical. Any unchanged parabromaniline was removed by distilling an alkaline solution with steam. The bromine was removed by boiling with zinc dust and alkali.³ Prolonged boiling was found to be necessary. After removing the zinc, the sulphonic acid was separated from the sodium chloride as described in the preceding section. The identity of the substance was positively confirmed by diazotization and conversion into orthoethoxybenzenesulphonamide, $C_6H_4(OC_2H_5)SO_2NH_2$, melting at 156° (uncorr.).⁴ On titration, 0.9 gram of the acid required 0.2914 gram of potassium hydroxide for neutralization, calculated 0.3919 gram.

Phenylglycocolloorthosulphonic Acid.

It was desired to prepare a sulphonic acid corresponding to

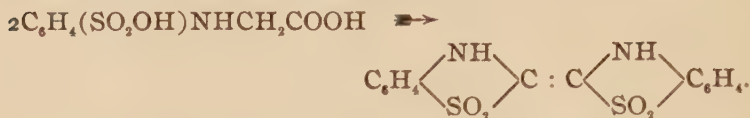
¹ Ann. Chem. (Liebig), **286**, 377.

² Hübner : *Ibid.*, **209**, 355.

³ Kreis : *Loc. cit.* Gerilowsky : Ber. d. chem. Ges., **29**, 1075.

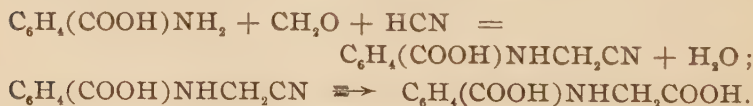
⁴ Franklin : Am. Chem. J., **20**, 462.

phenylglycocollorthocarboxylic acid and to condense it to a compound analogous to indigo, thus :



Attempts were made to condense anilineorthosulphonic acid with chloracetic acid, just as anthranilic acid condenses with chloracetic acid.¹ The proportions used correspond to those recommended for anthranilic acid. Ten grams of anilineorthosulphonic acid, 6.5 grams of chloracetic acid and 10.5 grams of sodium carbonate were dissolved in 320 cc. of water and the solution boiled for several hours, under a return condenser. The original acid was recovered unchanged. The same result was obtained when no sodium carbonate was added. The two acids were then heated, in aqueous solution, in a sealed tube, with and without the addition of sodium carbonate, at about 150°, for several hours. No evidence of condensation was detected. Bromacetic acid was then tried, with the same negative result. Similar attempts to condense sulphanilic acid with chloracetic acid also failed. Anthranilic acid condenses very readily. Orthonitraniline does not condense with chloracetic acid, but condenses readily with bromacetic acid.² The failure of the anilinesulphonic acids to condense with chloracetic acid is probably to be explained by the strongly negative character of the sulphonic acid group.

Phenylglycocollorthocarboxylic acid is easily prepared by the action of formic aldehyde and hydrocyanic acid on anthranilic acid, and hydrolysis of the resulting nitrile :³



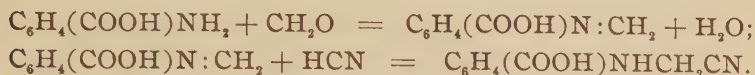
There are two steps in the first process, the condensation

¹ Mauthner and Suida : Monats. Chem., 9, 728. Heumann : Ber. d. chem. Ges., 23, 3432. German Imp. Pat., 56, 273.

² Plöchl : Ber. d. chem. Ges., 19, 7.

³ German Imp. Pat., 117, 924; 120, 105.

with formic aldehyde and the subsequent addition of hydrocyanic acid, thus :



This method was found to be very satisfactory when applied to anilineorthosulphonic acid. The following proportions were found to give the best results : Anilineorthosulphonic acid, 8.65 grams, was dissolved in 50 cc. of hot water, containing 3.25 grams of anhydrous potassium carbonate. Ten cc. of hydrochloric acid, sp. gr. 1.16 = 7.3 grams of HCl, were added, and then a concentrated solution of potassium cyanide, till the mixture became neutral to Congo red paper. It was now made slightly acid by means of a few drops of concentrated hydrochloric acid, whereupon 3.75 cc. of a 40 per cent solution of formic aldehyde were added and the mixture was warmed on the water-bath for about an hour. At the end of this time a concentrated solution of about 8 grams of potassium hydroxide was added and the solution was boiled until evolution of ammonia ceased. After cooling, it was mixed with enough hydrochloric acid to precipitate the phenylglycocoll orthosulphonic acid as the acid potassium salt, which is rather sparingly soluble in cold water. It dissolves in concentrated hydrochloric acid and the free sulphonic acid crystallizes out of the solution.

The materials from which this salt was obtained being comparatively difficult to prepare, most of the following experiments were made with parabromphenylglycocoll orthosulphonic acid. This was prepared in exactly the same way as the bromine-free compound, 12.6 grams of parabromaniline orthosulphonic acid being substituted for the 8.65 grams of aniline orthosulphonic acid. The acid potassium salt obtained in this way is very insoluble in cold water. It was recrystallized from hot water, from which it is deposited in needles. The salt contains water of crystallization, but loses it in varying amounts when dried in the air. A determination of potassium was made on a portion dried at 125°.

0.2932 gram salt gave 0.0722 gram K_2SO_4 .

	Calculated for $C_6H_3Br(SO_3OK)NHCH_2COOH$.	Found.
K	11.24	11.05

When a solution of this salt, in hot water, is rendered strongly acid with hydrochloric acid and allowed to cool slowly, the free sulphonic acid is deposited in flaky crystals. It is very soluble in water, much less soluble in a rather concentrated solution of hydrochloric acid. When titrated, 0.1119 gram required 0.0287 gram of sodium hydroxide for neutralization, calculated 0.0289 gram.

If the free acid, contaminated with potassium chloride, is dissolved in hot, absolute methyl alcohol, the solution filtered and evaporated to a rather small bulk, the acid is changed to an ester acid, which can be precipitated by the addition of ether. Analysis:

0.5841 gram substance gave 0.3369 gram AgBr.

	Calculated for $C_6H_3Br(SO_3OH)NHCH_2COOCH_3$.	Found.
Br	24.66	24.54

When titrated, 0.1708 gram of the ester acid required 0.0215 gram of sodium hydroxide for neutralization, calculated 0.0211 gram. The ester was saponified by boiling with an excess of a standard solution of sodium hydroxide. By titrating the excess of alkali, the amount consumed was determined. Total sodium hydroxide used for saponification and neutralization 0.0429 gram, calculated 0.0422 gram.

Attempts at Condensation.

1. Phenylglycocollorthocarboxylic acid is converted into indigo by fusing with sodium hydroxide at 250° – 300° , dissolving the resulting mass in water and passing air through the solution.¹ Since fused alkali at such a high temperature replaces the sulphonic acid group by phenolic hydroxyl, this method of condensation was not tried on parabromphenylglycocollorthosulphonic acid.

2. Phenylglycocoll is converted into indigodisulphonic acid by the action of fuming sulphuric acid.² Phenylglycocoll-

¹ Heumann: Ber. d. chem. Ges., **23**, 3432.

² Heumann: *Ibid.*, **24**, 1476, 3070. German Imp. Pat., **63**, 218; **68**, 372.

orthocarboxylic acid gives no indigo by this method, but it seemed desirable to try it on the corresponding sulphonic acid. Accordingly, 15 grams of acid potassium parabromphenylglycocollorthosulphonate were added, slowly, to 50 grams of fuming sulphuric acid, containing 20 per cent free sulphuric anhydride, the temperature being maintained below 40°. A considerable quantity of gas was evolved during the process of solution. The mixture was added to 100 grams of fuming sulphuric acid containing 80 per cent free sulphuric anhydride and allowed to stand for half an hour. The acid was then poured on ice. A white solid separated, which, on crystallization from hot water, was found to be parabromanilineorthosulphonic acid. Analysis:

0.5693 gram substance gave 0.4297 gram AgBr.

	Calculated for $C_6H_3Br(NH_2)SO_3OH$.	Found.
Br	32.11	31.71

0.3025 gram required 0.0478 gram sodium hydroxide for neutralization, calculated 0.0480 gram.

The fuming sulphuric acid removes the acetic acid portion of the molecule and probably oxidizes it to oxalic acid, which, of course, would appear as carbon monoxide and carbon dioxide. When phenylglycocollorthosulphonic acid is treated with fuming sulphuric acid it evolves gas just as the bromine derivative does.

3. Diacetylindoxyl, $C_6H_4 \begin{matrix} \diagup N(C_2H_5O) \\ \diagdown C(OC_2H_5O) \end{matrix} \rangle CH$, is very easily

prepared by heating the neutral sodium salt of phenylglycocollorthocarboxylic acid with acetic anhydride.¹ Carbon dioxide is evolved during the reaction and the product is insoluble in water. It is easily converted into indigo by boiling with dilute alkali. This method of condensation was tried on parabromphenylglycocollorthosulphonic acid by boiling 5 grams of the acid potassium salt with 1.5 grams of anhydrous sodium acetate and 25 grams of acetic anhydride for some time, under a return condenser. No carbon dioxide was

¹ German Imp. Pat., 113, 240.

evolved during the reaction. The acetic anhydride was distilled off under reduced pressure. The residue was very soluble in water. The solubility of the product, and the fact that no carbon dioxide was evolved made it seem very probable that the substance obtained was still a sulphonic acid and that the reaction had not gone beyond the acetylation of the imino group.

4. The neutral esters of phenylglycocollorthocarboxylic acid are very easily converted into esters of indoxylic acid by the action of sodium alcoholates.¹ Attempts were made to prepare neutral esters of parabromphenylglycocollorthosulphonic acid by the action of methyl iodide on the silver salt of the acid methyl ester, and by the action of dimethyl sulphate on the neutral sodium salt of the acid, but without success. No further experiments were made in this direction, as the condensation probably depends on the presence of the carbonyl group, like all Claisen condensations.

5. Sodamide has been used recently in place of sodium hydroxide in the preparation of indoxyl and indoxylic acid from phenylglycocollorthocarboxylic acid.² The application of this method to the sulphonic acid gave some promise of success, because the temperature required is lower, and the disturbing influence of the fused alkali on the sulphonic acid group is practically eliminated. The sodamide was prepared by the method of Dennis and Browne.³ No condensation product could be obtained, however, when acid potassium parabromphenylglycocollorthosulphonate was heated at about 200° with the sodamide, or at 250° with the sodamide diluted with potassium cyanide.

These methods, used in the preparation of indigo from phenylglycocollorthocarboxylic acid, having failed when applied to the corresponding sulphonic acid, further attempts to effect the condensation did not seem to be justified.

¹ Vorländer and Schilling: *Ann. Chem. (Liebig)*, **301**, 349.

² German Imp. Pat., **137**, 955.

³ *J. Am. Chem. Soc.*, **26**, 587.

BIOGRAPHY.

Hamilton Bradshaw was born at DeKalb, Illinois, December 31, 1881. He received his early education in the public and high schools of DeKalb, and entered Beloit College in the fall of 1898. He received the degree of Bachelor of Arts in June, 1902. In October, 1902, he entered the Johns Hopkins University as a graduate student in chemistry. His subordinate subjects have been physical chemistry and physics. In 1903-1904 he was a laboratory assistant to Dr. Gilpin, and in 1904-1905 he held a University fellowship in chemistry.

